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Characterizing zoonotic disease detection in the United States: Who detects zoonotic disease outbreaks & how fast are they detected?

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Summary There have been many calls for improved detection of zoonoses; research has not yet characterized zoonotic disease detection in the United States, in humans or animals. This research reviewed ''who detects'' zoonotic disease outbreaks and ''how fast'' they are detected. Definitions were operationalized based on existing literature and current practice. An outbreak database was created from publicly available records: Morbidity and Mortality Weekly Reports and ProMed-Mail. Univariate and bivariate statistics—including chi-square tests, Kruskal—Wallis tests, and Dunn's method were used for analysis. From an $n = 101$, results showed that laboratories (human health) detected 32.7% ($n = 33$) of the outbreaks; physicians/clinicians (human health) detected 18.8% ($n = 19$). The median time to was 13 days; mean was 31.7 (range = 0—492). There was a relationship between the type of the entity (laboratory, practitioner, or state agency) and how fast the outbreak was detected; state agencies were slower in detection. There was also a significant relationship between how fast an outbreak was detected and whether the outbreak occurred in multiple regions. This research provides important empirical evidence regarding U.S. zoonotic disease outbreak detection, highlighting the difficulty in rapid detection of multi-state outbreaks and the need for rapid, sensitive diagnostic testing and astute practitioners.

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Introduction

Zoonotic diseases are a significant threat to public health; approximately half of the 1700 pathogens that are known to infect humans are zoonoses [1,2]. However, the different states in the United States have widely varying requirements and capabilities for zoonotic disease outbreak detection and reporting [3—5]. Both public and private stakeholders have argued that improved zoonotic disease outbreak detection is critically important, and a systematic, federal integration of veterinary and human disease surveillance and reporting should be considered [6—8]. The existing literature has not yet presented empirical evidence describing the current characteristics of disease outbreak detection in the United States specifically for zoonoses.

This research, which is based on a database of disease outbreaks constructed by reviewing the publicly available literature from 1998 to 2008, empirically analyzed the characteristics of zoonotic disease outbreaks in the United States. In particular, it focused on who detected these outbreaks, how fast they were detected, and the relationship between these variables. Similar research has been conducted [9—11], but prior analyses have not specifically focused on zoonotic diseases or described the relationship between who detected the outbreak and the speed of detection.

Because of the disconnect between animal health and public health disease detection systems [6—8], as well as capability and policy differences between the states in the United States [5], this type of information is critical to obtain a better understanding of the factors that may delay zoonotic disease outbreak detection and thereby potentially threaten public health. The results presented in this manuscript provide empirical descriptive and quantitative information about the actual practice of zoonotic disease detection in the United States, and the results may inform public policy.

Methods

Identifying zoonotic diseases of interest

To identify zoonotic diseases of interest, three primary lists were consulted: the U.S. Centers for Disease Control and Prevention (CDC) Nationally Notifiable Disease List (all diseases that affect humans); the World Organization for Animal Health (OIE) Reportable Disease List (all diseases that affect animals); and a U.S. Department of Agriculture (USDA) list of wildlife disease agents of concern (all diseases that affect wild animals). All non-zoonotic diseases were immediately removed from the potential pool.

Subsequently, the following process was followed. First, any zoonotic disease listed on both the CDC and the OIE list was included. Second, any zoonotic disease listed on the USDA list and the CDC list was included. Third, all zoonoses from the CDC Category A, B, and C Bioterrorism Agents/Diseases list were included [12]. Fourth, peer-reviewed literature was evaluated to capture additional relevant diseases from a public health security perspective (i.e., those with concerning transmissibility characteristics or mortality rates, such as Ebola). Fifth, zoonotic diseases that scientists agree are not a threat to public health (such as vesicular stomatitis) were excluded. Sixth, a physician with specific expertise in zoonoses from The George Washington University Medical Center reviewed the tentative list and recommended 13 additional diseases, 8 of which were from the CDC Nationally Notifiable Disease List, that should be included.

Forty-one zoonoses of interest were ultimately identified (Table 1); these diseases were considered to be the most relevant from a biological, health security, and policy standpoint. Although some of the diseases on the list had never been detected in the United States, because of rapid travel, trade, transport and the documented permeability of international borders, these diseases were included.

Creating an outbreak database

The database was created in Excel, and drop-down menus with discrete choices were used to prevent coding errors.

Data sources

The data were collected from publicly available literature dated from 1998 to 2008. This date range was selected for two reasons: first, an extended period was required to ensure a sufficient sample size for statistical analysis, and second, modifications occurred to the U.S. CDC National Outbreak Reporting System in 2009, which resulted in significant changes to the scope and level of enteric disease outbreak reporting [13]. As such, the date range was truncated at 2008 to improve the validity of the results.

Federal-level data were used because disease outbreaks may cross jurisdictions and state reporting requirements vary for animals and humans [3—5]. Outbreaks that originated outside the United

Table 1 List of zoonotic diseases included in research.

Anthrax
Blastomycosis
Bovine Spongiform Encephalopthy (including variant Creutzfeldt Jacob Disease)
Bovine Tuberculosis
Brucellosis (multiple spp.)
Campylobacter
Coccidioidomycosis
Crimean-Congo Hemorrhagic Fever
Cryptococcosis
Ebola Hemorrhagic Fever
Ehrlichiosis/Anaplasmosis
Eastern Equine Encephalomyelitis
Glanders
Hantavirus
Histoplasmosis
Highly Pathogenic Avian Influenza
Japanese Encephalitis
Lassa Fever
Leishmaniasis
Leptospirosis
Lyme Disease
Malaria
Marburg
Monkeypox
Newcastle Disease Virus
Nipah/Hendra (Henipavirus)
Novel Influenza A Viruses
Plague
Psittacosis
Q Fever
Rabies
Rocky Mountain Spotted Fever
Rift Valley Fever
Salmonellosis
Shiga Toxin Producing *Escherichia coli*
St. Louis Encephalitis Virus
Trichinellosis
Tularemia
Venezuelan Equine Encephalomyelitis
West Nile Virus
Western Equine Encephalomyelitis

States but were detected within the United States were included.

The primary data sources were (1) the Morbidity and Mortality Weekly Reports (MMWR), a CDC official publication also used by Dato et al. [9], and (2) ProMed-Mail [14], a moderated open-source system that has been validated as a useful and accurate source of information in prior research, including in the study conducted by Cowen et al. [14].

From 1998 to 2008, all MMWR and ProMed-Mail records were searched for the diseases described in Section ''Identifying zoonotic diseases of interest''. After this step, additional data were collected from the annual report that the United States submits to the OIE, annual reports from the Nationally Notifiable Disease Surveillance System, and Weekly Epidemiological Reports produced by the World Health Organization (WHO). Google Scholar and Lexis Nexis were then used to capture further details about the outbreaks associated with detections that were previously identified by MMWR or ProMed-Mail.

Definitions

An outbreak was defined based on a combination of the WHO and OIE definitions [15,16]. The WHO defines an outbreak as

''the occurrence of cases of disease in excess of what would normally be expected in a defined community, geographical area, or season. An outbreak may occur in a restricted geographical area, or may extend over several countries. It may last for a few days or weeks, or for several years. A single case of a communicable disease long absent from a population, or caused by an agent (e.g., bacterium or virus) not previously recognized in that community or area, or the emergency of a previously unknown disease, may also constitute an outbreak and should be reported and investigated [15].''

The OIE defines an outbreak as ''the occurrence of one or more cases in an epidemiological unit'' [16].

For this study, an outbreak was operationalized as the occurrence of one or more cases in an epidemiological unit in excess of what is normally observed geographically, temporally, or in a specific population. Lab-acquired infections, intentionally dispersed agents, emerging agents, disease cases from novel transmission pathways, and cases of drug-resistant strains were also defined as outbreaks. This definition was similar to the definition used by Dato et al. [9] but slightly more inclusive to ensure that events of significant public health, animal health, economic, or security concern were captured.

''Who detects'' was defined as the individual or entity that first detected the outbreak (a confirmatory diagnostic of the causative agent was not required); this also has been referred to as initial detection or initial recognition [10]. The detection type in the cases in which a practitioner (animal or human) submitted a diagnostic sample to a laboratory without a presumptive diagnosis were considered laboratory detection, whereas type of detection associated with the cases in which the practitioner submitted a sample with a presumptive

diagnosis awaiting confirmatory diagnostics were considered practitioner detection.

''How fast'' was defined as the time from the presentation of the first clinical signs to the time that the outbreak was actually detected [9,10,17]. Clinical signs could be self-reported or identified by a practitioner. Despite the possibility of recall bias or reporting error, this was the most consistent information available across the outbreak data and avoided confounding the incubation period with timeliness.

Data fields and coding

A literal content analysis was conducted, and coding rules were developed for each of the variables. The outbreak database captured 22 pieces of information, including ''whether it was an outbreak'', ''who detected'', ''date of first case'', and ''date of initial recognition''; the latter two fields correspond to ''how fast'' a zoonotic disease outbreak was detected. The state in which the disease outbreak occurred was also included in the analysis.

The coding criteria ensured consistent coding of each outbreak from the primary data source into the outbreak database. For further data verification and validation, two secondary coders were used to validate that the outbreaks were coded consistently from the data sources to the database. Ten percent of the outbreaks ($n = 101$) were coded by the secondary coders, which resulted in the verification of 220 data points (10 outbreaks, 22 data points per outbreak). The primary coding was confirmed for 96.8% of the data points (213 of 220). The discordant coding was resolved through a small clarification in the criteria used for coding, which was then re-applied to the coding of each of the outbreaks in the database.

Statistics

SPSS and Minitab were used. Univariate statistics, including the median and mean times to detection and the frequency of outbreaks in species categories (domestic animals, humans, wildlife), were calculated. Bivariate analyses were conducted to analyze relationships between the variables, and the chi-square test (a non-directional test) was used due to the nominal data. The statistical significance was set at $\alpha = 0.05$, which is a customary level. These analyses did not determine causality, but explanatory power was gleaned in cases in which there was a temporal relationship between the variables.

Using the ''how fast'' data, Kruskal—Wallis tests were used to analyze the differences in the medians for different populations. Dunn's post hoc method was then used to isolate the group(s) that was (were) significantly different from the others via a multiple comparison procedure. Although the H-statistic used in this test was not as powerful as the parametric F-statistic, the Kruskal—Wallis test was more appropriate for the non-normal distributions and differing sample sizes between the groups.

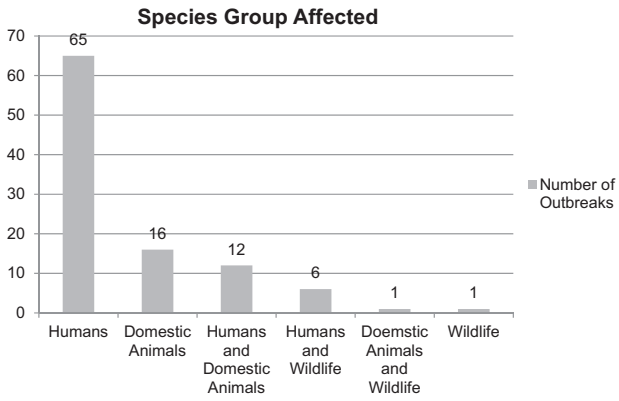

Figure 1 Species group affected by zoonotic disease outbreaks ($n = 101$).

Results

Four-hundred-and-forty outbreaks were captured in the database, and these outbreaks were distributed relatively evenly between 1998 and 2008. Salmonellosis was most common (86 outbreaks; 19.5%), followed by *E. coli* (Shiga Toxin-producing; 58 outbreaks; 13.2%), and anthrax and rabies (45 outbreaks each; 10.2%).

Outbreaks with ''who detects'' and ''how fast'' data

Of the 440 outbreaks, 171 (36.4%) included ''who detects'' data, 118 (25.1%) had ''how fast'' information, and 101 (21.5%) included both. These 101 outbreaks were further analyzed, and the results showed that they appeared in 42 states and the District of Columbia. Temporally, there was as few as one outbreak per year (1996 and 1997) to 15 per year (2006 and 2007).

Species affected and disease agents

Over half of the outbreaks (65; 64.4%) were documented only in humans, 16 of the outbreaks (15.8%) occurred only in domestic animals, and 12 of the outbreaks (11.9%) occurred in both humans and domestic animals (Fig. 1). Of these 101 disease outbreaks, rabies was the most common (19 outbreaks; 18.8%), followed by salmonellosis and anthrax

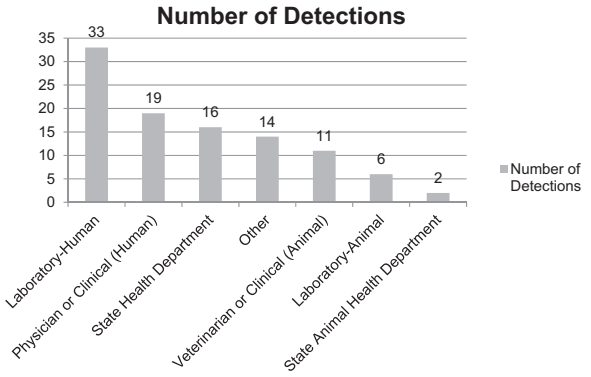

Figure 2 Who detected zoonotic disease outbreaks ($n = 101$).

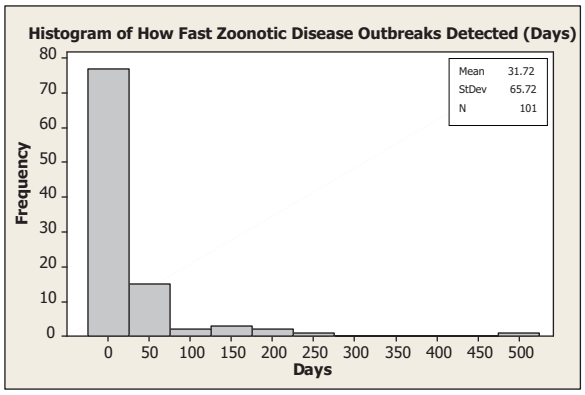

Figure 3 How fast zoonotic disease outbreaks were detected.

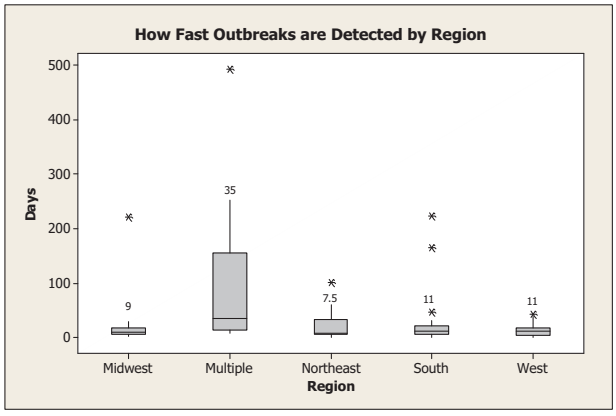

Figure 4 How fast zoonotic disease outbreaks were detected by region ($n = 101$; * indicates an outlier; median shown on boxplot).

(17 outbreaks each; 16.8%). Of the 41 diseases listed in Section ''Identifying zoonotic diseases of interest'', 25 diseases with complete ''who detects'' and ''how fast'' data were captured.

Who detects

The analysis of the categories of entities or individuals detected showed that human laboratory detections were most common (33 detections; 32.7%), followed by physicians/clinicians (19 detections; 18.8%), and State Health Departments (16 detections; 15.8%). In the ''other'' category (14 detections; 13.9%), county/city/district health departments, herd owners, or collaborative efforts were identified (Fig. 2).

The human and animal entities were collapsed and then differentiated by entity type: laboratories (either animals or human) detected 41 outbreaks (46.1%), practitioners (veterinarians, physicians, and other clinical practitioners) detected 30 outbreaks (33.7%), and state departments detected 18 outbreaks (17.8%). The ''other'' category was excluded from this analysis ($n = 89$).

How fast

Out of the 101 identified outbreaks, the minimum time to outbreak detection was 0 days, which indicates that detection occurred on the same day that clinical signs were first reported, and the maximum time was 492 days. The results of this analysis showed a mean of 31.7 days and a median of 13 days. Fig. 3 presents a histogram of these data ($n = 101$). The standard deviation was 65.7, mainly due to nine high-value outliers. After removing these outliers ($n = 92$), the standard deviation decreased to 12.61, with a mean of 14.5. The distribution of these data was not normal (using the Anderson–Darling test, AD-statistic = 19.897).

At the ''fast'' end of the scale were outbreaks of rabies (detected at 0 days) and of *E. coli* (detected at 1 day), and at the ''slow'' end of the scale were two multi-state outbreaks of salmonellosis, which were detected at 492 and 251 days, respectively.

''How fast'' data analyzed by region of occurrence. To understand whether the location at which the outbreak occurred impacted the speed of outbreak detection, the ''how fast'' data were analyzed by region. ''How fast'' was statistically related ($p = 0.008$, H-statistic = 13.78) to whether the disease outbreak occurred in multiple regions (as observed in Fig. 4). Even after the outlier was removed (492 days), the result was still significant ($p = 0.019$, H-statistic = 10.77).[2] Dunn's method showed a statistically significant difference between the multiple and Midwest groups and between the multiple and West groups ($p < 0.05$; Q-value = 3.052 and 3.026, respectively).

[2] Additional outliers were not removed to maintain a larger sample size for Dunn's post hoc comparison.

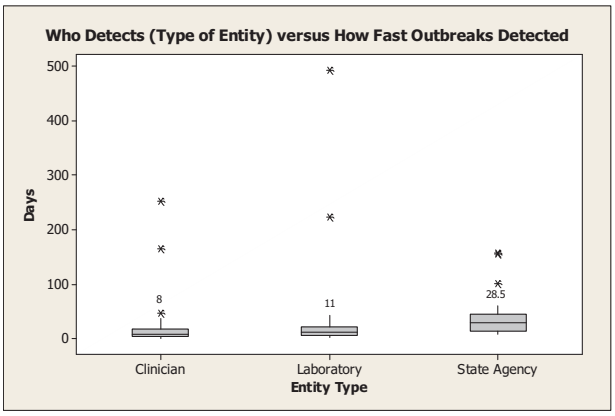

Figure 5 Who detected (type of entity) versus how fast the outbreak was detected ($n = 89$; * indicates an outlier; median shown on boxplot).

Relationship between ''who detects'' and ''how fast'' data

A further analysis was performed to characterize the relationship between the ''who detects'' and ''how fast'' data. As determined using the Kruskall—Wallis test, there was not a statistically significant relationship between the entity that detected (all seven entities listed in Fig. 2) and the time to detection: the H-statistic was 10.77, and the p value was 0.096.

Relationship between ''who detects'' and ''how fast'' data for different types of entities

Even when the categories were collapsed due to small sample sizes into three groups by sector (animal entity, human entity, and other), the results were not statistically significant (H-statistic = 1.30; p value = 0.522). There was no significant difference between the ''how fast'' data for zoonotic disease outbreaks detected by animal health entities and the ''how fast'' data for zoonotic disease outbreaks detected by human health entities.

The ''who detects'' categories were collapsed by entity type rather than by sector into state agencies ($n = 18$); physician; veterinarian, and clinician ($n = 30$); and laboratory ($n = 41$). The ''other'' data were excluded, resulting in $n = 89$ because they were not easily collapsible into the previous categories. Fig. 5 shows the results of the analysis of the ''how fast'' data by the ''who detects'' data and the entity type.

The results of the Kruskal—Wallis test were significant: H-statistic = 13.51 and p value = 0.001. The null hypothesis that the medians of these groups were equal was rejected, indicating that the type of entity that detected a zoonotic disease outbreak was related to ''how fast'' the outbreak was detected. Dunn's method was used to assess the differences between these groups, and the results revealed significant differences ($p < 0.05$; Q-statistic) between state agency and clinician and between state agency and laboratory. As observed in Fig. 5, the median time to detection for state agencies was significantly higher than that for the other entities.

Discussion

These results provide the first characterization of zoonotic disease outbreaks in the United States from 1998 to 2008. The predominance of human-only outbreaks and detections in these data was not surprising given the focus on human health in the literature. Human health entities, including physicians/clinicians, state public health departments, human disease laboratories, and local or county health departments, detected 72.3% of the outbreaks captured. It may be useful to note that in the United States, rabies (which accounted for 19 outbreaks) is typically within the jurisdiction of public health departments, even when detected in animals.

When reviewed by entity type, this research produced results similar to those reported by Ashford et al. [10], who cited that 36.3% of outbreak recognitions and reportings originated from health care professionals or infectious disease practitioners. In this study, 33.7% of the outbreaks were detected by clinicians, physicians, and veterinarians. However, both Dato et al. [9] and Ashford et al. [10] reported a higher percentage of outbreaks detected by state health departments: 53% and 30.5% respectively, in comparison to 17.8% in this research. In large part, these differences are likely due to the different definitions of initial detection in each of these studies. Neither Dato et al. nor Ashford et al. attempted to disaggregate laboratory detection into a category and instead subsumed laboratory detection under state health departments or practitioners depending on who subsequently identified the outbreak or notified authorities when the diagnostics were complete. Additionally, the prior research studies have not focused specifically on zoonoses [9—11].

The median time to detection ($n = 101$) was 13 days, which—considering that these data included hard-to-detect outbreaks of foodborne diseases—was encouraging. Given the outliers, the median was significantly higher (31.7 days). The number of outbreaks that were quickly detected was surprising for zoonoses given the concern regarding the disconnect between animal health and human

health surveillance and detection systems. However, these results were aligned with prior findings.

Although direct comparisons are difficult due to sampling differences, Dato et al. [9] showed a cluster of outbreaks detected within the first 7 days, which was also observed in this research (the first quartile was 6 days). Chan et al. [11] cited an average of 15 days to event detection, which was similar to the mean of 14.5 presented in this research after the outliers were removed. The results reported by Ashford et al. [10] also indicated rapid initial recognition, with only 0—26 days between the beginning of an outbreak and the time at which an individual or institution identified the problem. The congruity of the results presented here with those in the existing literature reinforces their reliability.

One of the most significant findings was that the type of entity but not the sector was related to the median time to zoonotic disease outbreak detection. In other words, there was not a statistically significant difference between how quickly human health entities and animal health entities detected zoonotic disease outbreaks. Given the concern over the disparate funding and focus on disease surveillance strategies and systems between the animal health and human health sectors, this was a positive finding [6—8]. Prior research studies have not attempted to associate who detected the outbreak with how fast the outbreak was detected.

The analysis of the entity type showed that clinicians detected outbreaks more quickly than state departments and that laboratories made the detections faster than state departments. This is not surprising because laboratories perform detections based on diagnostic confirmation, which can take time to perform. State agencies detected outbreaks more slowly because they were typically aggregators of broader surveillance data; a higher incidence level in space or time may have been necessary to trigger recognition, further investigation, and subsequently detection.

Zoonotic disease outbreaks that occurred in more than one region were found to be detected more slowly than disease outbreaks that occurred in a single region. This is largely due to the outlying foodborne disease outbreaks, which took significant time to detect. Based on these results, it remains clear that multi-state foodborne outbreaks, despite advances in the analysis of subtyping data and the rapid, automated collation of this information, were harder to detect because cases often occurred gradually and over a wide geographical area.

This evidence highlights the importance and necessity of practitioner education (both physician and veterinarian) to detect zoonotic disease outbreaks; these individuals are the first line of defense for the protection of both public health and animal health. Additionally, the role of both human and animal laboratories in zoonotic disease detection indicates the necessity of rapid, specific, and sensitive laboratory tests for fast recognition.

Limitations

A key limitation of this research study was that there is an unknown denominator: the number of zoonotic disease outbreaks that appeared in the data sources is obviously not the same as the number of outbreaks that actually occurred; thus, overgeneralization of these results should be avoided because individuals and states may elect not to report disease cases and disease outbreaks may or may not be detected in the first place. Despite this limitation, this study provides the first characterization of zoonotic disease outbreak detection in the United States, and the results can be used to inform further research.

There was some possible bias toward rapid detection for diseases with acute symptoms because clinicians may have identified these more rapidly and individuals may have been more likely to recall their clinical signs. Additionally, this approach to the definition of timeliness may have disadvantaged animals, which cannot recall the first sign of disease and rely on astute herd owners, managers, and veterinarians. However, further analysis was performed, and there was no relationship between the primary symptom of the disease and the median days to detection ($p = 0.872$); subsequently, this limitation should not be viewed as a significant threat to the validity and reliability of these results.

Conclusions

These findings provide the first characterization of zoonotic disease outbreak detection in the United States. In particular, this research study presents critical empirical information with regard to who detected the identified outbreaks, how rapidly they were detected, and the relationship between these two variables. This information is needed to inform more complex qualitative and quantitative research, as well as policy, on zoonotic disease outbreak detection in the United States.

Overall, the general rapidness of outbreak detection suggests that the surveillance and detection systems, even though they are disparate and disconnected, may be more effective than previously described in theory. However, in cases with

a highly contagious zoonotic disease, the need for rapid detection, reporting, and response cannot be overstated.

Further research should be conducted on the timeliness of formal reporting (and potentially the response) rather than just detection, i.e., the time at which the disease is formally reported to a state or federal entity and when or if there was any response. Additional analyses, perhaps using private records, may also be of value to provide a better understanding the reporting completeness of zoonotic diseases in both human and animal populations in the United States.

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Competing interests

None declared.

Ethical approval

Not required.

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